IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Walke *et al.*		
Serial No.:	09/818,990	Group Art Unit:	1652
Filed:	3/27/2001	Examiner:	S. Swope

For: Novel Human Muscle Proteins and Polynucleotides Encoding the Same (As Previously Amended)

Attorney Docket No.: LEX-0152-USA

APPEAL BRIEF

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APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed on May 27, 2003. The Notice of Appeal was timely submitted on August 25, 2003, and was received in the Patent and Trademark Office ("the Office") on September 2, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of one month to and including December 2, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(1) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief ($165.00), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

The present application was filed on March 27, 2001, claiming the benefit of U.S. Provisional Application Number 60/192,218, which was filed on March 27, 2000, and included original claims 1-5. A Restriction and Election Requirement was issued on October 2, 2002, separating the original claims into two separate and distinct inventions. In a response to the Restriction and Election Requirement submitted to the Office on November 4, 2002, Appellants elected without traverse to prosecute the claims of the Group I invention (original claims 1-3) for prosecution on the merits, cancelled claims 4 and 5 without prejudice and without disclaimer as drawn to a non-elected invention, amended claim 2 to further improve its clarity, and added new claims 6-10.

A First Official Action on the merits ("the First Action") was issued on December 27, 2002, in which the title and abstract of the application were objected to, claims 1-3 and 6-10 were rejected under 35 U.S.C. § 101 as allegedly lacking a patentable utility, claim 2 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, claims 1, 7 and 10 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claims 1, 7 and 10 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, claim 1 was rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hillier *et al.* (GenBank Database Accession Number AA179499; "Hillier"), and claims 7 and 10 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hillier in view of Ausubel (1987, *Current Protocols in Molecular Biology*, Chapter 16; "Ausubel") and further in view of Zheng (1990, *Nature* **344**:556-559; "Zheng"). In a response to the First Official Action submitted to the Office on March 26, 2003 ("Response to the First Action"), Appellants amended the title of the application, amended claims 1 to specifically recite an isolated nucleic acid molecule comprising at least 2000 contiguous bases of nucleotide sequence first disclosed in SEQ ID NO:1 and amended claim 2 to even further improve its clarity, and addressed the objection to the abstract and the various rejections of claims 1-3 and 6-10.

A Second and Final Official Action ("the Final Action") was issued on May 27, 2003, indicating that the objection to the title and the abstract, and the rejections of claim 2 under 35 U.S.C. § 112, second

paragraph, as allegedly indefinite, claims 1, 7 and 10 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claims 7 and 10 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, claim 1 under 35 U.S.C. § 102(b) as allegedly anticipated by Hillier, and claims 7 and 10 under 35 U.S.C. § 103(a) as allegedly unpatentable over Hillier in view of Ausubel and further in view of Zheng had been overcome by the amendments and remarks submitted in the Response to the First Action, maintaining the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and setting forth a new rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. In a response to the Final Action submitted to the Office on August 25, 2003 ("Response to the Final Action"), Appellants addressed the rejections of claims 1-3 and 6-10.

An Advisory Action ("the Advisory Action") was mailed on November 17, 2003, maintaining the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and although not specifically addressing these rejections, apparently maintaining the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, and claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Therefore, claims 1-3 and 6-10 are the subject of this appeal. A copy of the appealed claims are included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

As no amendments subsequent to the Final Action have been filed, Appellants believe that no outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human polynucleotide sequences that encode a novel protein that shares structural similarity with mammalian muscle proteins (specification at page 2, lines 1-3), and particularly titan-like protein (specification at page 2, line 9 and page 16, line 11).

The presently claimed polynucleotide sequences were compiled from clustered human gene trapped sequences, genomic sequence, ESTs, and cDNAs isolated from a human muscle cDNA library (specification at page 16, lines 4-6). Four coding single nucleotide polymorphisms were identified in the claimed sequence - specifically, a C/G polymorphism at nucleotide position 1684 of SEQ ID NO:1, which can result in a leucine or phenylalanine being present at corresponding amino acid position 628 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2072 of SEQ ID NO:1, which can result in a serine or asparagine being present at corresponding amino acid position 691 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2120 of SEQ ID NO:1, which can result in an asparagine or serine being present at corresponding amino acid position 707 of SEQ ID NO:2; and an A/G polymorphism at nucleotide position 2540 of SEQ ID NO:1, which can result in a glycine or glutamate being present at corresponding amino acid position 847 of SEQ ID NO:2 (specification at page 16, lines 10-24).

The specification details a number of uses for the presently claimed polynucleotide sequences, including in diagnostic assays such as forensic analysis (see, for example, the specification at page 11, line 9), in the identification of coding sequence (see, for example, the specification at page 2, lines 30-32), in mapping a unique gene to a particular chromosome (see, for example, the specification at page 2, lines 32-33), and in assessing gene expression patterns, particularly using a high throughput "chip" format (see, for example, the specification from page 5, line 32 to page 6, line 2).

VI. ISSUES ON APPEAL

1. Do claims 1-3 and 6-10 lack a patentable utility?
2. Are claims 1-3 and 6-10 unusable by a skilled artisan due to a lack of patentable utility?
3. Does claim 1 lack sufficient written description?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, associated with the utility rejection, the claims will stand or fall together. For the purposes of the outstanding rejection under 35 U.S.C. § 112, first paragraph, associated with written description, claim 1 will stand or fall alone.

VIII. ARGUMENT

A. Do Claims 1-3 and 6-10 Lack a Patentable Utility?

The Final Action first rejects claims 1-3 and 6-10 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial or a well-established utility.

Appellants pointed out both in the Response to the First Action and the Response to the Final Action that the present nucleic acid sequences have utility in diagnostic assays, such as forensic analysis, as described in the specification as originally filed (see, for example, page 11, line 9). As described in the specification at page 16, lines 10-24, the presently claimed sequence defines four coding single nucleotide polymorphisms - specifically, a C/G polymorphism at nucleotide position 1684 of SEQ ID NO:1, which can result in a leucine or phenylalanine being present at corresponding amino acid position 628 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2072 of SEQ ID NO:1, which can result in a serine or asparagine being present at corresponding amino acid position 691 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2120 of SEQ ID NO:1, which can result in an asparagine or serine being present at corresponding amino acid position 707 of SEQ ID NO:2; and an A/G polymorphism at nucleotide position 2540 of SEQ ID NO:1, which can result in a glycine or glutamate being present at corresponding amino acid position 847 of SEQ ID NO:2. As such polymorphisms are the basis for forensic analysis, which in undoubtedly a "real world" utility, the presently claimed sequence must in itself be useful.

Appellants respectfully point out that the presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to distinguish individual members of the human population from one another based simply on the presence or absence

of one or more of the described polymorphisms. The skilled artisan would be able to use the presently described polymorphisms in forensic analysis exactly as they were described in the specification as originally filed, without any additional research. It is important to note that simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain these polymorphic markers does not mean that additional research is needed in order for these markers as they are presently described in the instant specification to be used in forensic science.

This is also not a case of a potential utility. Even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population). Appellants point out that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Appellants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Appellants respectfully point out that all that is required to support Appellants' assertion of utility is for the skilled artisan to believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Appellants every day provides more than ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Appellants in the same fashion. Therefore, the presently claimed sequence clearly has a substantial and well established utility.

The Final Action questioned this asserted utility, stating "the presence of polymorphisms in human DNA is well established and virtually any locus on a human chromosome will exhibit one or more polymorphisms which could be so used" (the Final Action at page 3). Appellants pointed out in the Response to the Final Action that this argument is flawed in a **number** of respects. First, until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is **meaningless**. The Examiner appears to be attempting to use

the information presented for the first time by Appellants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such hindsight analysis based on Appellants discovery is completely improper. Second, the Examiner is clearly confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. The fact that other polymorphic markers have been identified in other genetic loci, or that the use of the presently described polymorphic markers will provide additional information concerning the prevalence of these markers in certain subpopulations, does not mean that use of the polymorphic markers identified by Appellants' in SEQ ID NO:1 in forensic analysis is not a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

In other words, just because other (possibly better) polymorphic markers from the human genome have been described, or that additional information about the presently described polymorphic markers can be gained through the use of these markers, does not establish that the presently described polymorphic markers lack a specific utility. Importantly, the holding in the *Carl Zeiss* case is **mandatory legal authority** that essentially controls the outcome of the present case. This case, and particularly the cited quote, **directly** rebuts the Examiner's argument, which is presumably why the Examiner failed to address the holding of *Carl Zeiss* in both the Final Action and the Advisory Action. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of

golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. In view of the above standards and "common sense" analysis, there can be little question that the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Furthermore, Appellants pointed out in the Response to the Final Action as the presently described polymorphisms are a part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through

> research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis as described in the specification as originally filed, without the need for any further research. As discussed above, even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic marker as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Again, as a matter of law, it is well settled that a patent need not disclose what is well known in the art (*In re Wands, supra*).

Importantly, it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As set forth in *In re Langer* (183 USPQ 288 (CCPA 1974); "*Langer*"):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as

> sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, absent such evidence from the Examiner concerning the use of the presently described polymorphisms in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Additionally, in both the Response to the First Action and the Response to the Final Action, Appellants pointed out that a sequence sharing nearly 100% percent identity at the protein level over the entire length of the claimed sequence was present in the leading scientific repository for biological sequence data (GenBank), and had been annotated by third party scientists *wholly unaffiliated with Appellants* as "Homo sapiens myopalladin" (GenBank accession number AF328296; alignment and GenBank report shown in **Exhibit A**). Additionally, Appellants pointed out that myopalladin has been shown by these scientists to be involved in muscle structure (Bang *et al.*, *J. Cell Biol.* **153**:413-427, 2001; **Exhibit B**). In the Final Action the Examiner stated that "(b)ased on the alignment of the protein encoded by SEQ ID NO:1 with GenBank Acc# AF328296 and the report of Bang et al, (*sic*) 2001, the identity of said protein as myopalladin is credible", but that "this argument constitutes only hindsight reasoning" that "lacks any assertion of function" (the Final Action bridging pages 3 and 4). Appellants respectfully disagree. In the specification as originally filed, Appellants described the described sequences as "structural proteins" (specification at page 1, line 10; see also page 1, lines 21-22), specifically "muscle proteins" (specification at page 2, line 3) and more specifically "titin-like protein" (specification at page 2, line 9, and page 16, line 11). Appellants pointed out that titin is a structural component of muscle that was well-known at the time the present application was filed, as evidenced by more than 100 publications in PubMed published prior to the March 27, 2000 priority date of the present application that include "titin" in the title. Thus, the function of the presently claimed sequence as a muscle structural protein was clearly asserted by Appellants in the specification as originally filed, which is all that is required to satisfy the requirements of 35 U.S.C. § 101. The citation of GenBank accession number AF328296 and the Bang *et al.* article

merely **confirm** Appellants assertion of utility as set forth in the specification as originally filed. As set forth repeatedly by Appellants, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation and reference, there can be no question that those skilled in the art would clearly believe that Appellants' sequence is a muscle structural protein. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner further questions Appellants assertion of utility in the Advisory Action, because "no specific cellular processes mediated by said protein or diseases cause (*sic*) by mutation of said protein have been disclosed by the specification" (the Advisory Action at page 2). Appellants first point out that the association of a nucleotide sequence with a particular type of disease is **not** the standard for patentability under 35 U.S.C. § 101. As detailed above, in *In re Brana, (supra)*, the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. Furthermore, Appellants point out that this argument has no bearing on the patentable utility of the present claims, for it has long been established that "[I]t is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works" (*In re Cortright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999), quoting *Newman v. Quiqq*, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989)). See also *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed. Cir. 1983) ("[I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests"). Thus, the Examiner's arguments are completely without merit, and in no way support the alleged lack of utility.

Therefore, while Appellants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes a muscle structural protein, the Examiner has provided no evidence that directly establishes that the specifically claimed sequence does not encode a muscle structural protein. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility. Furthermore, Appellants respectfully point out that the PTO itself does not require 100% identity between proteins to establish functional homology.

Example 10 of the Revised Interim Utility Guidelines Training Materials (**Exhibit** C) only requires a similarity score greater than 95% to establish functional homology. Therefore, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law.

Although Appellants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), in both the Response to the First Action and the Response to the Final Action, Appellants detailed an additional example of the utility of the present nucleotide sequences, as described in the specification from page 5, line 32 to page 6, line 2, specifically that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit** D), 5,556,752 (**Exhibit** E), 5,744,305 (**Exhibit** F), 5,837,832 (**Exhibit** G), 6,156,501 (**Exhibit** H) and 6,261,776 (**Exhibit** I). Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies that have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section VIII(B), below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are

associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action also questioned this utility, stating that "Applicants have also not identified any particular reason for use of this particular polynucleotide in 'DNA chips'" (the Final Action at page 3). First, Appellants point out that nucleic acid sequences are commonly used in gene chip applications without **any** information regarding the function of the encoded protein, or even evidence regarding whether the sequence is actually even expressed. Thus, the present sequence, which has been biologically validated to be expressed, has a much greater utility than sequences that are merely predicted to be expressed based on bioinformatic analysis. Additionally, Appellants point out that nucleic acid sequences such as SEQ ID NO:1 are routinely used by companies throughout the biotechnology sector **exactly** as they are presented in the Sequence Listing, without **any** further experimentation. Expression profiling does **not** require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Furthermore, although further information regarding the biological activity of a particular nucleic acid sequence might make it even more useful in gene chip applications, this does not mean that the use of the presently claimed nucleic acid sequence in gene chip applications is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). The fact that other expressed sequences can be used to track gene expression, or that additional information concerning the presently claimed sequence might make it even more useful in certain gene chip embodiments, does not mean that the use of Appellants' sequence to track gene expression on a gene chip is not a specific utility. Therefore, this argument also fails to support the alleged lack of utility of the presently claimed compositions.

Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see,

e.g., Venter *et al.*, 2001, Science *291*:1304; **Exhibit J**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit K**. Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As yet a further example of the utility of the presently claimed polynucleotide, Appellants noted in the Response to the First Action and the Response to the Final Action that the present nucleotide sequence has a specific utility in "identification of coding sequence" (specification at page 2, lines 30-32) and in "determining the genomic structure" of the protein encoding regions of the corresponding human chromosome (specification at page 11, line 8). This is evidenced by the fact that SEQ ID NO:1 can be used to map the 19 coding exons on chromosome 10 (present within three overlapping chromosome 10 clones; GenBank Accession Numbers AC024258, AL512429 and AC016395; alignments and the first page from each of the GenBank reports are presented in **Exhibit L**). Appellants respectfully remind the Board that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). It is well known that intron/exon boundaries are mutational hot spots, and thus the identification of the actual splice sites is of great utility to the skilled artisan. Such biologically validated splice junctions are superior to splice junctions that may have been predicted from genomic sequence alone, and, as detailed in the specification, at least at page 11, lines 9-14, that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics". Appellants respectfully

submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

As an additional example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 2, lines 32-33, the present nucleotide sequences have a specific utility in "mapping a unique gene to a particular chromosome". This is evidenced by the fact that SEQ ID NO:1 can be used to map the 19 coding exons on chromosome 10, as detailed above (**Exhibit** 𝕃). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 10 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325; **Exhibit** 𝕁, which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner also questioned these asserted utilities, because "applicants have not identified any particular reason for identifying the coding sequence or using this polynucleotide in mapping chromosome 10" (the Final Action at page 3), and because such uses "would apply to every member of a general class of materials" (the Advisory Action at page 2). As there is no further guidance in the Advisory Action, Appellants are left to guess as to which "general class of materials" the Examiner is referring. Nevertheless, these arguments do not support the alleged lack of utility of the presently claimed compositions. Appellants first point out that only those small percentage of nucleotide sequences that are

located in this region of chromosome 10 can be used in such a manner. Second, the Examiner is once again confusing the requirements of a **specific** utility with a **unique** utility. The fact that a small number of other nucleotide sequences could be used to map the protein coding regions in this specific region of chromosome 10 does not mean that the use of Appellants' sequence to map the protein coding regions of chromosome 10 is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*).

Regarding the utility requirements under 35 U.S.C. § 101, the Federal Circuit has clearly stated "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)). Thus, based on the relevant case law, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, While Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the

new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit M**), 5,654,173 (**Exhibit N**), and 5,552,281 (**Exhibit O**; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit P**; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants understand that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1-3 and 6-10 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in Section VIII(A) concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana, supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1-3 and 6-10 have been shown to have "a specific, substantial, and credible utility", as detailed in Section VIII(A) above, the

present rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph, must be overruled.

C. Does Claim 1 Lack Sufficient Written Description?

The Final Action next rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Final Action stated that the specification "is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus" (the Final Action bridging pages 5 and 6). The Examiner seems to be requiring a complete and exact description of every member of the claimed genus in order to comply with the requirements of 35 U.S.C. § 112, first paragraph. Appellants respectfully point out that this is **not** the standard for compliance with 35 U.S.C. § 112, first paragraph. Appellants further point out that there is **no requirement whatsoever** that novel fragments of a novel sequence have the **exact same function** as the full length sequence in order to be patented. If this were to be the case, hundreds, if not thousands, of issued U.S. Patents would be instantly invalidated, as they each claim nucleotide fragments that have not been demonstrated to have the exact same function as the full length nucleotide sequence. Appellants therefore submit that the claimed sequence meets the written description requirement of 35 U.S.C. § 112, first paragraph.

As set forth by Appellants in the Response to the First Action and the Response to the Final Action, 35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*" *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Appellants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Regents of Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not

> define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Regents of Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to **distinguish** the claimed nucleic acids from other materials on the basis of the specific **structural** description provided. Polynucleotides comprising at least 2000 contiguous bases from SEQ ID NO:1 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. The claimed genus of polynucleotides is clearly defined in structural terms, which is **all that is required** of claim 1 to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

For each of the foregoing reasons, Appellants submit that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. (Previously Presented) An isolated nucleic acid molecule comprising at least 2000 contiguous bases of nucleotide sequence first disclosed in SEQ ID NO: 1.

2. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

3. (Original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

6. (Previously Presented) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

7. (Previously Presented) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 1.

8. (Previously Presented) The recombinant expression vector of claim 7, wherein the isolated nucleic acid molecule encodes the amino acid sequence shown in SEQ ID NO:2.

9. (Previously Presented) The recombinant expression vector of claim 8, wherein the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO: 1.

10. (Previously Presented) A host cell comprising the recombinant expression vector of claim 7.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1-3 and 6-10 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility, and that claim 1 lacks sufficient written description, is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

December 2, 2003
Date

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TABLE OF AUTHORITIES

CASES

STATUTES

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Walke *et al.*		
Serial No.:	09/818,990	Group Art Unit:	1652
Filed:	3/27/2001	Examiner:	S. Swope

For: Novel Human Muscle Proteins and Polynucleotides Encoding the Same (As Previously Amended)

Attorney Docket No.: LEX-0152-USA

APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed on May 27, 2003. The Notice of Appeal was timely submitted on August 25, 2003, and was received in the Patent and Trademark Office ("the Office") on September 2, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of one month to and including December 2, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(1) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief ($165.00), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

The present application was filed on March 27, 2001, claiming the benefit of U.S. Provisional Application Number 60/192,218, which was filed on March 27, 2000, and included original claims 1-5. A Restriction and Election Requirement was issued on October 2, 2002, separating the original claims into two separate and distinct inventions. In a response to the Restriction and Election Requirement submitted to the Office on November 4, 2002, Appellants elected without traverse to prosecute the claims of the Group I invention (original claims 1-3) for prosecution on the merits, cancelled claims 4 and 5 without prejudice and without disclaimer as drawn to a non-elected invention, amended claim 2 to further improve its clarity, and added new claims 6-10.

A First Official Action on the merits ("the First Action") was issued on December 27, 2002, in which the title and abstract of the application were objected to, claims 1-3 and 6-10 were rejected under 35 U.S.C. § 101 as allegedly lacking a patentable utility, claim 2 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, claims 1, 7 and 10 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claims 1, 7 and 10 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, claim 1 was rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hillier *et al.* (GenBank Database Accession Number AA179499; "Hillier"), and claims 7 and 10 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hillier in view of Ausubel (1987, *Current Protocols in Molecular Biology*, Chapter 16; "Ausubel") and further in view of Zheng (1990, *Nature* **344**:556-559; "Zheng"). In a response to the First Official Action submitted to the Office on March 26, 2003 ("Response to the First Action"), Appellants amended the title of the application, amended claims 1 to specifically recite an isolated nucleic acid molecule comprising at least 2000 contiguous bases of nucleotide sequence first disclosed in SEQ ID NO: 1 and amended claim 2 to even further improve its clarity, and addressed the objection to the abstract and the various rejections of claims 1-3 and 6-10.

A Second and Final Official Action ("the Final Action") was issued on May 27, 2003, indicating that the objection to the title and the abstract, and the rejections of claim 2 under 35 U.S.C. § 112, second

paragraph, as allegedly indefinite, claims 1, 7 and 10 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claims 7 and 10 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, claim 1 under 35 U.S.C. § 102(b) as allegedly anticipated by Hillier, and claims 7 and 10 under 35 U.S.C. § 103(a) as allegedly unpatentable over Hillier in view of Ausubel and further in view of Zheng had been overcome by the amendments and remarks submitted in the Response to the First Action, maintaining the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and setting forth a new rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. In a response to the Final Action submitted to the Office on August 25, 2003 ("Response to the Final Action"), Appellants addressed the rejections of claims 1-3 and 6-10.

An Advisory Action ("the Advisory Action") was mailed on November 17, 2003, maintaining the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and although not specifically addressing these rejections, apparently maintaining the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, and claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Therefore, claims 1-3 and 6-10 are the subject of this appeal. A copy of the appealed claims are included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

As no amendments subsequent to the Final Action have been filed, Appellants believe that no outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human polynucleotide sequences that encode a novel protein that shares structural similarity with mammalian muscle proteins (specification at page 2, lines 1-3), and particularly titan-like protein (specification at page 2, line 9 and page 16, line 11).

The presently claimed polynucleotide sequences were compiled from clustered human gene trapped sequences, genomic sequence, ESTs, and cDNAs isolated from a human muscle cDNA library (specification at page 16, lines 4-6). Four coding single nucleotide polymorphisms were identified in the claimed sequence - specifically, a C/G polymorphism at nucleotide position 1684 of SEQ ID NO:1, which can result in a leucine or phenylalanine being present at corresponding amino acid position 628 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2072 of SEQ ID NO:1, which can result in a serine or asparagine being present at corresponding amino acid position 691 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2120 of SEQ ID NO:1, which can result in an asparagine or serine being present at corresponding amino acid position 707 of SEQ ID NO:2; and an A/G polymorphism at nucleotide position 2540 of SEQ ID NO:1, which can result in a glycine or glutamate being present at corresponding amino acid position 847 of SEQ ID NO:2 (specification at page 16, lines 10-24).

The specification details a number of uses for the presently claimed polynucleotide sequences, including in diagnostic assays such as forensic analysis (see, for example, the specification at page 11, line 9), in the identification of coding sequence (see, for example, the specification at page 2, lines 30-32), in mapping a unique gene to a particular chromosome (see, for example, the specification at page 2, lines 32-33), and in assessing gene expression patterns, particularly using a high throughput "chip" format (see, for example, the specification from page 5, line 32 to page 6, line 2).

VI. ISSUES ON APPEAL

1. Do claims 1-3 and 6-10 lack a patentable utility?
2. Are claims 1-3 and 6-10 unusable by a skilled artisan due to a lack of patentable utility?
3. Does claim 1 lack sufficient written description?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, associated with the utility rejection, the claims will stand or fall together. For the purposes of the outstanding rejection under 35 U.S.C. § 112, first paragraph, associated with written description, claim 1 will stand or fall alone.

VIII. ARGUMENT

A. Do Claims 1-3 and 6-10 Lack a Patentable Utility?

The Final Action first rejects claims 1-3 and 6-10 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial or a well-established utility.

Appellants pointed out both in the Response to the First Action and the Response to the Final Action that the present nucleic acid sequences have utility in diagnostic assays, such as forensic analysis, as described in the specification as originally filed (see, for example, page 11, line 9). As described in the specification at page 16, lines 10-24, the presently claimed sequence defines four coding single nucleotide polymorphisms - specifically, a C/G polymorphism at nucleotide position 1684 of SEQ ID NO:1, which can result in a leucine or phenylalanine being present at corresponding amino acid position 628 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2072 of SEQ ID NO:1, which can result in a serine or asparagine being present at corresponding amino acid position 691 of SEQ ID NO:2; an A/G polymorphism at nucleotide position 2120 of SEQ ID NO:1, which can result in an asparagine or serine being present at corresponding amino acid position 707 of SEQ ID NO:2; and an A/G polymorphism at nucleotide position 2540 of SEQ ID NO:1, which can result in a glycine or glutamate being present at corresponding amino acid position 847 of SEQ ID NO:2. As such polymorphisms are the basis for forensic analysis, which in undoubtedly a "real world" utility, the presently claimed sequence must in itself be useful.

Appellants respectfully point out that the presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to distinguish individual members of the human population from one another based simply on the presence or absence

of one or more of the described polymorphisms. The skilled artisan would be able to use the presently described polymorphisms in forensic analysis exactly as they were described in the specification as originally filed, without **any** additional research. It is important to note that simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain these polymorphic markers does not mean that additional research is needed in order for these markers as they are presently described in the instant specification to be used in forensic science.

This is also not a case of a potential utility. Even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population). Appellants point out that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Appellants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Appellants respectfully point out that all that is required to support Appellants' assertion of utility is for the skilled artisan to believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Appellants every day provides more than ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Appellants in the same fashion. Therefore, the presently claimed sequence clearly has a substantial and well established utility.

The Final Action questioned this asserted utility, stating "the presence of polymorphisms in human DNA is well established and virtually any locus on a human chromosome will exhibit one or more polymorphisms which could be so used" (the Final Action at page 3). Appellants pointed out in the Response to the Final Action that this argument is flawed in a **number** of respects. First, until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is **meaningless**. The Examiner appears to be attempting to use

the information presented for the first time by Appellants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such hindsight analysis based on Appellants discovery is completely improper. Second, the Examiner is clearly confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. The fact that other polymorphic markers have been identified in other genetic loci, or that the use of the presently described polymorphic markers will provide additional information concerning the prevalence of these markers in certain subpopulations, does not mean that use of the polymorphic markers identified by Appellants' in SEQ ID NO:1 in forensic analysis is not a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

In other words, just because other (possibly better) polymorphic markers from the human genome have been described, or that additional information about the presently described polymorphic markers can be gained through the use of these markers, does not establish that the presently described polymorphic markers lack a specific utility. Importantly, the holding in the *Carl Zeiss* case is **mandatory legal authority** that essentially controls the outcome of the present case. This case, and particularly the cited quote, **directly** rebuts the Examiner's argument, which is presumably why the Examiner failed to address the holding of *Carl Zeiss* in both the Final Action and the Advisory Action. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of

golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. In view of the above standards and "common sense" analysis, there can be little question that the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Furthermore, Appellants pointed out in the Response to the Final Action as the presently described polymorphisms are a part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through

> research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis as described in the specification as originally filed, without the need for any further research. As discussed above, even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic marker as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Again, as a matter of law, it is well settled that a patent need not disclose what is well known in the art (*In re Wands, supra*).

Importantly, it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As set forth in *In re Langer* (183 USPQ 288 (CCPA 1974); "*Langer*"):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as

> sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, absent such evidence from the Examiner concerning the use of the presently described polymorphisms in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Additionally, in both the Response to the First Action and the Response to the Final Action, Appellants pointed out that a sequence sharing nearly 100% percent identity at the protein level over the entire length of the claimed sequence was present in the leading scientific repository for biological sequence data (GenBank), and had been annotated by third party scientists *wholly unaffiliated with Appellants* as "Homo sapiens myopalladin" (GenBank accession number AF328296; alignment and GenBank report shown in **Exhibit A**). Additionally, Appellants pointed out that myopalladin has been shown by these scientists to be involved in muscle structure (Bang *et al.*, *J. Cell Biol.* **153**:413-427, 2001; **Exhibit B**). In the Final Action the Examiner stated that "(b)ased on the alignment of the protein encoded by SEQ ID NO:1 with GenBank Acc# AF328296 and the report of Bang et al, (*sic*) 2001, the identity of said protein as myopalladin is credible", but that "this argument constitutes only hindsight reasoning" that "lacks any assertion of function" (the Final Action bridging pages 3 and 4). Appellants respectfully disagree. In the specification as originally filed, Appellants described the described sequences as "structural proteins" (specification at page 1, line 10; see also page 1, lines 21-22), specifically "muscle proteins" (specification at page 2, line 3) and more specifically "titin-like protein" (specification at page 2, line 9, and page 16, line 11). Appellants pointed out that titin is a structural component of muscle that was well-known at the time the present application was filed, as evidenced by more than 100 publications in PubMed published prior to the March 27, 2000 priority date of the present application that include "titin" in the title. Thus, the function of the presently claimed sequence as a muscle structural protein was clearly asserted by Appellants in the specification as originally filed, which is all that is required to satisfy the requirements of 35 U.S.C. § 101. The citation of GenBank accession number AF328296 and the Bang *et al.* article

merely **confirm** Appellants assertion of utility as set forth in the specification as originally filed. As set forth repeatedly by Appellants, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation and reference, there can be no question that those skilled in the art would clearly believe that Appellants' sequence is a muscle structural protein. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner further questions Appellants assertion of utility in the Advisory Action, because "no specific cellular processes mediated by said protein or diseases cause (*sic*) by mutation of said protein have been disclosed by the specification" (the Advisory Action at page 2). Appellants first point out that the association of a nucleotide sequence with a particular type of disease is **not** the standard for patentability under 35 U.S.C. § 101. As detailed above, in *In re Brana, (supra)*, the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. Furthermore, Appellants point out that this argument has no bearing on the patentable utility of the present claims, for it has long been established that "[I]t is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works" (*In re Cortright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999), quoting *Newman v. Quiqq*, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989)). See also *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed. Cir. 1983) ("[I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests"). Thus, the Examiner's arguments are completely without merit, and in no way support the alleged lack of utility.

Therefore, while Appellants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes a muscle structural protein, the Examiner has provided no evidence that directly establishes that the specifically claimed sequence does not encode a muscle structural protein. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility. Furthermore, Appellants respectfully point out that the PTO itself does not require 100% identity between proteins to establish functional homology.

Example 10 of the Revised Interim Utility Guidelines Training Materials (**Exhibit C**) only requires a similarity score greater than 95% to establish functional homology. Therefore, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law.

Although Appellants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), in both the Response to the First Action and the Response to the Final Action, Appellants detailed an additional example of the utility of the present nucleotide sequences, as described in the specification from page 5, line 32 to page 6, line 2, specifically that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit D**), 5,556,752 (**Exhibit E**), 5,744,305 (**Exhibit F**), 5,837,832 (**Exhibit G**), 6,156,501 (**Exhibit H**) and 6,261,776 (**Exhibit I**). Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies that have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section VIII(B), below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are

associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action also questioned this utility, stating that "Applicants have also not identified any particular reason for use of this particular polynucleotide in 'DNA chips'" (the Final Action at page 3). First, Appellants point out that nucleic acid sequences are commonly used in gene chip applications without **any** information regarding the function of the encoded protein, or even evidence regarding whether the sequence is actually even expressed. Thus, the present sequence, which has been biologically validated to be expressed, has a much greater utility than sequences that are merely predicted to be expressed based on bioinformatic analysis. Additionally, Appellants point out that nucleic acid sequences such as SEQ ID NO:1 are routinely used by companies throughout the biotechnology sector **exactly** as they are presented in the Sequence Listing, without **any** further experimentation. Expression profiling does **not** require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Furthermore, although further information regarding the biological activity of a particular nucleic acid sequence might make it even more useful in gene chip applications, this does not mean that the use of the presently claimed nucleic acid sequence in gene chip applications is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). The fact that other expressed sequences can be used to track gene expression, or that additional information concerning the presently claimed sequence might make it even more useful in certain gene chip embodiments, does not mean that the use of Appellants' sequence to track gene expression on a gene chip is not a specific utility. Therefore, this argument also fails to support the alleged lack of utility of the presently claimed compositions.

Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see,

e.g., Venter *et al.*, 2001, Science *291*:1304; **Exhibit J**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit K**. Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As yet a further example of the utility of the presently claimed polynucleotide, Appellants noted in the Response to the First Action and the Response to the Final Action that the present nucleotide sequence has a specific utility in "identification of coding sequence" (specification at page 2, lines 30-32) and in "determining the genomic structure" of the protein encoding regions of the corresponding human chromosome (specification at page 11, line 8). This is evidenced by the fact that SEQ ID NO:1 can be used to map the 19 coding exons on chromosome 10 (present within three overlapping chromosome 10 clones; GenBank Accession Numbers AC024258, AL512429 and AC016395; alignments and the first page from each of the GenBank reports are presented in **Exhibit L**). Appellants respectfully remind the Board that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). It is well known that intron/exon boundaries are mutational hot spots, and thus the identification of the actual splice sites is of great utility to the skilled artisan. Such biologically validated splice junctions are superior to splice junctions that may have been predicted from genomic sequence alone, and, as detailed in the specification, at least at page 11, lines 9-14, that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics". Appellants respectfully

submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

As an additional example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 2, lines 32-33, the present nucleotide sequences have a specific utility in "mapping a unique gene to a particular chromosome". This is evidenced by the fact that SEQ ID NO:1 can be used to map the 19 coding exons on chromosome 10, as detailed above (**Exhibit L**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 10 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325; **Exhibit J**, which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner also questioned these asserted utilities, because "applicants have not identified any particular reason for identifying the coding sequence or using this polynucleotide in mapping chromosome 10" (the Final Action at page 3), and because such uses "would apply to every member of a general class of materials" (the Advisory Action at page 2). As there is no further guidance in the Advisory Action, Appellants are left to guess as to which "general class of materials" the Examiner is referring. Nevertheless, these arguments do not support the alleged lack of utility of the presently claimed compositions. Appellants first point out that only those small percentage of nucleotide sequences that are

located in this region of chromosome 10 can be used in such a manner. Second, the Examiner is once again confusing the requirements of a **specific** utility with a **unique** utility. The fact that a small number of other nucleotide sequences could be used to map the protein coding regions in this specific region of chromosome 10 does not mean that the use of Appellants' sequence to map the protein coding regions of chromosome 10 is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*).

Regarding the utility requirements under 35 U.S.C. § 101, the Federal Circuit has clearly stated "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)). Thus, based on the relevant case law, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, While Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the

new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit M**), 5,654,173 (**Exhibit N**), and 5,552,281 (**Exhibit O**; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit P**; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants understand that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1-3 and 6-10 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in Section VIII(A) concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana, supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1-3 and 6-10 have been shown to have "a specific, substantial, and credible utility", as detailed in Section VIII(A) above, the

present rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1-3 and 6-10 under 35 U.S.C. § 112, first paragraph, must be overruled.

C. Does Claim 1 Lack Sufficient Written Description?

The Final Action next rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Final Action stated that the specification "is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus" (the Final Action bridging pages 5 and 6). The Examiner seems to be requiring a complete and exact description of every member of the claimed genus in order to comply with the requirements of 35 U.S.C. § 112, first paragraph. Appellants respectfully point out that this is **not** the standard for compliance with 35 U.S.C. § 112, first paragraph. Appellants further point out that there is **no requirement whatsoever** that novel fragments of a novel sequence have the **exact same function** as the full length sequence in order to be patented. If this were to be the case, hundreds, if not thousands, of issued U.S. Patents would be instantly invalidated, as they each claim nucleotide fragments that have not been demonstrated to have the exact same function as the full length nucleotide sequence. Appellants therefore submit that the claimed sequence meets the written description requirement of 35 U.S.C. § 112, first paragraph.

As set forth by Appellants in the Response to the First Action and the Response to the Final Action, 35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*" *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Appellants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Regents of Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not

> define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Regents of Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to **distinguish** the claimed nucleic acids from other materials on the basis of the specific **structural** description provided. Polynucleotides comprising at least 2000 contiguous bases from SEQ ID NO:1 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. The claimed genus of polynucleotides is clearly defined in structural terms, which is **all that is required** of claim 1 to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

For each of the foregoing reasons, Appellants submit that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. (Previously Presented) An isolated nucleic acid molecule comprising at least 2000 contiguous bases of nucleotide sequence first disclosed in SEQ ID NO: 1.

2. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

3. (Original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

6. (Previously Presented) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

7. (Previously Presented) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 1.

8. (Previously Presented) The recombinant expression vector of claim 7, wherein the isolated nucleic acid molecule encodes the amino acid sequence shown in SEQ ID NO:2.

9. (Previously Presented) The recombinant expression vector of claim 8, wherein the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO: 1.

10. (Previously Presented) A host cell comprising the recombinant expression vector of claim 7.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1-3 and 6-10 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility, and that claim 1 lacks sufficient written description, is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

December 2, 2003
Date

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TABLE OF AUTHORITIES

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